

SEQUENCE LISTING

<110> Jensen, Michael

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<301> Collart, F.R. and Huberman, E.

<302> Cloning and sequence analysis of the human and

<303> J. Biol. Chem. (1988)

<304> 263

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<303> J. Biol. Chem. (1997)
<304> 271

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Ser Leu Leu Ala Ala Thr Thr Glu Ala Pro Gly Glu	Tyr Phe Phe Ser		
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Asp Gly Ile Arg Leu Lys Lys Tyr Arg Gly Met	Gly Ser Leu Asp Ala		
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Lys Ile Lys Val Ala Gln Gly Val Ser Gly Ala Val	Gln Asp Lys Gly		
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 <303> J. Biol. Chem. (1997)
 <304> 272
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 <306> 961-965

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Ser Pro Met Asp Thr Val Thr Glu Ala Gly Met Ala Ile Ala Met Ala			
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 Val Asp Leu Thr Ser Ala Leu Thr Lys Lys Ile Thr Leu Lys Thr Pro
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 Pro Glu Phe Gln Ala Asn Glu Val Arg Lys Val Lys Lys Tyr Glu Gln
 100 105 110
 Gly Phe Ile Thr Asp Pro Val Val Leu Ser Pro Lys Asp Arg Val Arg
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 Thr Asp Thr Gly Arg Met Gly Ser Arg Leu Val Gly Ile Ile Ser Ser
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 Arg Asp Ile Asp Phe Leu Lys Glu Glu His Asp Cys Phe Leu Glu
 165 170 175
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 Thr Leu Lys Glu Ala Asn Glu Ile Leu Gln Arg Ser Lys Lys Gly Lys
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 Leu Pro Ile Val Asn Glu Asp Asp Glu Leu Val Ala Ile Ile Ala Arg
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 Thr Asp Leu Lys Lys Asn Arg Asp Tyr Pro Leu Ala Ser Lys Asp Ala
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 245 250 255
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<301> Farazi et al.
<302> Isolation and Characterization of Mycophenolic
<303> J. Biol. Chem. (1997)
<304> 272
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Glu Gly Val His Ser Leu His Ser Tyr Glu Lys Arg Leu Phe				
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Leu Val Ser Ser Pro Met Asp Thr Val Thr Glu Ala Gly Met Ala Ile				
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Gly	Val	Val
100	105	110
Pro	Leu	Ile
115	120	125
Leu	His	His
130	135	140
Ile	Gly	Tyr
145	150	155
Leu	Asp	Asp
165	170	175
His	Gly	Gly
180	185	190
Asp	Gly	Gly
195	200	205
Leu	Asn	Pro
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Ile	Arg	Ile
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Gly	Tyr	Asp
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Ala	Ala	Ala
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Lys	Gln	Arg
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Asp	Tyr	Val
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Val	Val	Asn
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Ala	Asn	Val
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Asn	Arg	Thr
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Val	Asp	Asp
370	375	380
Asp	Gly	Asp
385	390	395
Pro	Pro	Ile
405	410	415
Leu	Gly	Pro
420	425	430
Asp	Ser	Gly
435	440	445
Ser	Gly	Asp
450	455	460
Asn	Asn	Val
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<300>
 <301> Natsumeda et al.
 <302> Two Distinct cDNAs for Human IMP Dehydrogenase
 <303> J. Biol. Chem. (1990)
 <304> 265
 <305> 9
 <306> 5292-5295

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<300>
 <301> Minet, M., Dufour, M-E., and Lacroote, F.
 <302> Cloning and Sequencing of a Human cDNA coding for
 <303> Gene (1992)
 <304> 121
 <306> 393-396

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Asn Pro Arg Pro Arg Val	Phe Arg Leu Pro	Glu Asp Gln Ala Val Ile			
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Asn Arg Tyr Gly Phe	Asn Ser His	Gly Leu Ser Val Val	Glu His Arg		
145	150	155	160		
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165	170	175			
cct ctg ggg gtc	aac ttg	ggg aag	aac aag	acc tca gtg	576
Pro Leu Gly Val	Asn Leu Gly	Lys Asn Lys	Thr Ser Val	Asp Ala Ala	
180	185	190			
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Glu Asp Tyr Ala	Gly Val Arg	Val Leu Gly	Pro Leu Ala	Asp Tyr	

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Arg Asp Gly Leu Arg Arg Val His Arg Pro Ala Val	Leu Val Lys Ile		
245	250	255	
gct cct gac ctc acc agc cag gat aag gag gac att	gcc agt gtg gtc		816
Ala Pro Asp Leu Thr Ser Gln Asp Lys Glu Asp Ile	Ala Ser Val Val		
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Lys Glu Leu Gly Ile Asp Gly Leu Ile Val Thr Asn	Thr Thr Val Ser		
275	280	285	
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Arg Pro Ala Gly Leu Gln Gly Ala Leu Arg Ser Glu	Thr Gly Gly Leu		
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Ser Gly Lys Pro Leu Arg Asp Leu Ser Thr Gln Thr	Ile Arg Glu Met		
305	310	315	320
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Tyr Ala Leu Thr Gln Gly Arg Val Pro Ile Ile Gly	Val Gly Gly Val		
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Ser Ser Gly Gln Asp Ala Leu Glu Lys Ile Arg Ala	Gly Ala Ser Leu		
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atcatgagag gagggactcc atcttgagcc atgtccccca	gcctggcatg cgtgcactgt		1318
aaacgccaat cgggggtca ccaggatcaa ccgcaggctt	tcttcagtc cttgggtcaga		1378
ccataaaactg cattttgtat tctttgtgga ttcaaaccct	aggatccatc agtcttgcaa		1438
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<400> 20			

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 Gly Asp Glu Arg Phe Tyr Ala Glu His Leu Met Pro Thr Leu Gln Gly
 35 40 45
 Leu Leu Asp Pro Glu Ser Ala His Arg Leu Ala Val Arg Phe Thr Ser
 50 55 60
 Leu Gly Leu Leu Pro Arg Ala Arg Phe Gln Asp Ser Asp Met Leu Glu
 65 70 75 80
 Val Arg Val Leu Gly His Lys Phe Arg Asn Pro Val Gly Ile Ala Ala
 85 90 95
 Gly Phe Asp Lys His Gly Glu Ala Val Asp Gly Leu Tyr Lys Met Gly
 100 105 110
 Phe Gly Phe Val Glu Ile Gly Ser Val Thr Pro Lys Pro Gln Glu Gly
 115 120 125
 Asn Pro Arg Pro Arg Val Phe Arg Leu Pro Glu Asp Gln Ala Val Ile
 130 135 140
 Asn Arg Tyr Gly Phe Asn Ser His Gly Leu Ser Val Val Glu His Arg
 145 150 155 160
 Leu Arg Ala Arg Gln Gln Lys Gln Ala Lys Leu Thr Glu Asp Gly Leu
 165 170 175
 Pro Leu Gly Val Asn Leu Gly Lys Asn Lys Thr Ser Val Asp Ala Ala
 180 185 190
 Glu Asp Tyr Ala Glu Gly Val Arg Val Leu Gly Pro Leu Ala Asp Tyr
 195 200 205
 Leu Val Val Asn Val Ser Ser Pro Asn Thr Ala Gly Leu Arg Ser Leu
 210 215 220
 Gln Gly Lys Ala Glu Leu Arg Arg Leu Leu Thr Lys Val Leu Gln Glu
 225 230 235 240
 Arg Asp Gly Leu Arg Arg Val His Arg Pro Ala Val Leu Val Lys Ile
 245 250 255
 Ala Pro Asp Leu Thr Ser Gln Asp Lys Glu Asp Ile Ala Ser Val Val
 260 265 270
 Lys Glu Leu Gly Ile Asp Gly Leu Ile Val Thr Asn Thr Thr Val Ser
 275 280 285
 Arg Pro Ala Gly Leu Gln Gly Ala Leu Arg Ser Glu Thr Gly Gly Leu
 290 295 300
 Ser Gly Lys Pro Leu Arg Asp Leu Ser Thr Gln Thr Ile Arg Glu Met
 305 310 315 320
 Tyr Ala Leu Thr Gln Gly Arg Val Pro Ile Ile Gly Val Gly Val
 325 330 335
 Ser Ser Gly Gln Asp Ala Leu Glu Lys Ile Arg Ala Gly Ala Ser Leu
 340 345 350
 Val Gln Leu Tyr Thr Ala Leu Thr Phe Trp Gly Pro Pro Val Val Gly
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<210> 21
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 <213> Homo sapien

<220>
 <221> CDS
 <222> (1)...(1101)
 <223> DHODH Truncated 39 kDa Construct

<300>

<301> Copeland, R.A., et al.
 <302> Recombinant Human Dihydroorotate Dehydrogenase
 <303> Arch. Biochem. Biophys. (1995)
 <304> 323
 <306> 79-86

<400> 21

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1	5				10							15				

ctg	cag	ggg	ctg	ctg	gac	ccg	gag	tca	gcc	cac	aga	ctg	gct	gtt	cgc	96
Leu	Gln	Gly	Leu	Leu	Asp	Pro	Glu	Ser	Ala	His	Arg	Leu	Ala	Val	Arg	
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ttc	acc	tcc	ctg	ggg	ctc	ctt	cca	cg	gcc	aga	ttt	caa	gac	tct	gac	144
Phe	Thr	Ser	Leu	Gly	Leu	Leu	Pro	Arg	Ala	Arg	Phe	Gln	Asp	Ser	Asp	
35			40					45								

atg	ctg	gaa	gtg	aga	gtt	ctg	ggc	cat	aaa	ttc	cga	aat	cca	gta	gga	192
Met	Leu	Glu	Val	Arg	Val	Leu	Gly	His	Lys	Phe	Arg	Asn	Pro	Val	Gly	
50		55				60										

att	gct	gca	gga	ttt	gac	aag	cat	ggg	gaa	gcc	gtg	gac	gga	ctt	tat	240
Ile	Ala	Ala	Gly	Phe	Asp	Lys	His	Gly	Glu	Ala	Val	Asp	Gly	Leu	Tyr	
65		70		75			80									

aag	atg	ggc	ttt	ggt	ttt	gtt	gag	ata	gga	agt	gtg	act	cca	aaa	cct	288
Lys	Met	Gly	Phe	Gly	Phe	Val	Glu	Ile	Gly	Ser	Val	Thr	Pro	Lys	Pro	
85		90				95										

cag	gaa	gga	aac	cct	aga	ccc	aga	gtc	ttc	cg	ctc	cct	gag	gac	caa	336
Gln	Glu	Gly	Asn	Pro	Arg	Pro	Arg	Val	Phe	Arg	Leu	Pro	Glu	Asp	Gln	
100		105				110										

gct	gtc	att	aac	agg	tat	gga	ttt	aac	agt	cac	ggg	ctt	tca	gtg	gtg	384
Ala	Val	Ile	Asn	Arg	Tyr	Gly	Phe	Asn	Ser	His	Gly	Leu	Ser	Val	Val	
115		120			125											

gaa	cac	agg	tta	cg	gg	cc	ag	cag	cag	g	cc	aag	ctc	aca	gaa	432
Glu	His	Arg	Leu	Arg	Ala	Arg	Gln	Gln	Lys	Gln	Ala	Lys	Leu	Thr	Glu	
130		135			140											

gat	gga	ctg	cct	ctg	ggg	gtc	aac	ttg	ggg	aag	aac	aag	acc	tca	gtg	480
Asp	Gly	Leu	Pro	Leu	Gly	Val	Asn	Leu	Gly	Lys	Asn	Lys	Thr	Ser	Val	
145		150			155		160									

gac	gcc	g	gag	gac	tac	gca	gaa	ggg	gt	cg	gt	gg	cc	ct	528	
Asp	Ala	Ala	Glu	Asp	Tyr	Ala	Glu	Gly	Val	Arg	Val	Leu	Gly	Pro	Leu	
165		170		175												

gcc	gac	tac	ctg	gt	gt	aat	gt	tcc	ag	cc	aa	act	g	gg	ct	576
Ala	Asp	Tyr	Leu	Val	Val	Asn	Val	Ser	Ser	Pro	Asn	Thr	Ala	Gly	Leu	
180		185		190												

cgg	agc	ctt	cag	gga	aag	gcc	gag	ctg	cg	cg	ctg	ctg	acc	aag	gt	624
Arg	Ser	Ieu	Gln	Gly	Lys	Ala	Glu	Leu	Arg	Arg	Leu	Leu	Thr	Lys	Val	
195		200		205												

ctg	cag	gag	agg	gat	ggc	ttg	cg	aga	gt	ca	gg	cc	g	tc	ct	672
Leu	Gln	Glu	Arg	Asp	Gly	Ieu	Arg	Arg	Val	His	Arg	Pro	Ala	Val	Leu	
210		215		220												

gtg aag atc gct cct gac ctc acc agc cag gat aag gag gac att gcc	720
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225 230 235 240	
agt gtg gtc aaa gag ttg ggc atc gat ggg ctg att gtt acg aac acc	768
Ser Val Val Lys Glu Leu Gly Ile Asp Gly Leu Ile Val Thr Asn Thr	
245 250 255	
acc gtg agt cgc cct gcg ggc ctc cag ggt gcc ctg cgc tct gaa aca	816
Thr Val Ser Arg Pro Ala Gly Leu Gln Gly Ala Leu Arg Ser Glu Thr	
260 265 270	
gga ggg ctg agt ggg aag ccc ctc cgg gat tta tca act caa acc att	864
Gly Gly Leu Ser Gly Lys Pro Leu Arg Asp Leu Ser Thr Gln Thr Ile	
275 280 285	
cgg gag atg tat gca ctc acc caa ggc cga gtt ccc ata att ggg gtt	912
Arg Glu Met Tyr Ala Leu Thr Gln Gly Arg Val Pro Ile Ile Gly Val	
290 295 300	
ggt ggt gtg agc agc ggg cag gac gcg ctg gag aag atc cgg gca ggg	960
Gly Gly Val Ser Ser Gly Gln Asp Ala Leu Glu Lys Ile Arg Ala Gly	
305 310 315 320	
gcc tcc ctg gtg cag ctg tac acg gcc ctc acc ttc tgg ggg cca ccc	1008
Ala Ser Leu Val Gln Leu Tyr Thr Ala Leu Thr Phe Trp Gly Pro Pro	
325 330 335	
gtt gtg ggc aaa gtc aag cgg gaa ctg gag gcc ctt ctg aaa gag cag	1056
Val Val Gly Lys Val Lys Arg Glu Leu Glu Ala Leu Leu Lys Glu Gln	
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35 40 45	
Met Leu Glu Val Arg Val Leu Gly His Lys Phe Arg Asn Pro Val Gly	
50 55 60	
Ile Ala Ala Gly Phe Asp Lys His Gly Glu Ala Val Asp Gly Leu Tyr	
65 70 75 80	
Lys Met Gly Phe Gly Phe Val Glu Ile Gly Ser Val Thr Pro Lys Pro	
85 90 95	
Gln Glu Gly Asn Pro Arg Pro Arg Val Phe Arg Leu Pro Glu Asp Gln	
100 105 110	
Ala Val Ile Asn Arg Tyr Gly Phe Asn Ser His Gly Leu Ser Val Val	
115 120 125	
Glu His Arg Leu Arg Ala Arg Gln Gln Lys Gln Ala Lys Leu Thr Glu	
130 135 140	

Asp Gly Leu Pro Leu Gly Val Asn Leu Gly Lys Asn Lys Thr Ser Val
 145 150 155 160
 Asp Ala Ala Glu Asp Tyr Ala Glu Gly Val Arg Val Leu Gly Pro Leu
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 Ala Asp Tyr Leu Val Val Asn Val Ser Ser Pro Asn Thr Ala Gly Leu
 180 185 190
 Arg Ser Leu Gln Gly Lys Ala Glu Leu Arg Arg Leu Leu Thr Lys Val
 195 200 205
 Leu Gln Glu Arg Asp Gly Leu Arg Arg Val His Arg Pro Ala Val Leu
 210 215 220
 Val Lys Ile Ala Pro Asp Leu Thr Ser Gln Asp Lys Glu Asp Ile Ala
 225 230 235 240
 Ser Val Val Lys Glu Leu Gly Ile Asp Gly Leu Ile Val Thr Asn Thr
 245 250 255
 Thr Val Ser Arg Pro Ala Gly Leu Gln Gly Ala Leu Arg Ser Glu Thr
 260 265 270
 Gly Gly Leu Ser Gly Lys Pro Leu Arg Asp Leu Ser Thr Gln Thr Ile
 275 280 285
 Arg Glu Met Tyr Ala Leu Thr Gln Gly Arg Val Pro Ile Ile Gly Val
 290 295 300
 Gly Gly Val Ser Ser Gly Gln Asp Ala Leu Glu Lys Ile Arg Ala Gly
 305 310 315 320
 Ala Ser Leu Val Gln Leu Tyr Thr Ala Leu Thr Phe Trp Gly Pro Pro
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 <222> 79
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 <223> A to C mutation

<221> CDS
 <222> (4)...(1101)
 <223> His26Ala DHODH mutant

<300>
 <301> Davis et al.
 <302> Histidine to Alanine mutants of Human Dihydroorotate
 <303> Biochem. Pharmacol. (1997)
 <304> 54
 <306> 459-465

<400> 23
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 Leu Gln Gly Leu Leu Asp Pro Glu Ser Ala Ala Arg Leu Ala Val Arg
 20 25 30

ttc acc tcc ctg ggg ctc ctt cca cgg gcc aga ttt caa gac tct gac Phe Thr Ser Leu Gly Leu Leu Pro Arg Ala Arg Phe Gln Asp Ser Asp	144
35 40 45	
atg ctg gaa gtt ctg ggc cat aaa ttc cga aat cca gta gga Met Leu Glu Val Arg Val Leu Gly His Lys Phe Arg Asn Pro Val Gly	192
50 55 60	
att gct gca gga ttt gac aag cat ggg gaa gcc gtg gac gga ctt tat Ile Ala Ala Gly Phe Asp Lys His Gly Glu Ala Val Asp Gly Leu Tyr	240
65 70 75	
aag atg ggc ttt ggt ttt gtt gag ata gga agt gtg act cca aaa cct Lys Met Gly Phe Gly Val Glu Ile Gly Ser Val Thr Pro Lys Pro	288
80 85 90 95	
cag gaa gga aac cct aga ccc aga gtc ttc cgc ctc cct gag gac caa Gln Glu Gly Asn Pro Arg Pro Arg Val Phe Arg Leu Pro Glu Asp Gln	336
100 105 110	
gct gtc att aac agg tat gga ttt aac agt cac ggg ctt tca gtg gtg Ala Val Ile Asn Arg Tyr Gly Phe Asn Ser His Gly Leu Ser Val Val	384
115 120 125	
gaa cac agg tta cgg gcc aga cag cag aag cag gcc aag ctc aca gaa Glu His Arg Leu Arg Ala Arg Gln Gln Lys Gln Ala Lys Leu Thr Glu	432
130 135 140	
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145 150 155	
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180 185 190	
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195 200 205	
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210 215 220	
gtg aag atc gct cct gac ctc acc agc cag gat aag gag gac att gcc Val Lys Ile Ala Pro Asp Leu Thr Ser Gln Asp Lys Glu Asp Ile Ala	720
225 230 235	
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240 245 250 255	
acc gtg agt cgc cct gcg ggc ctc cag ggt gcc ctg cgc tct gaa aca Thr Val Ser Arg Pro Ala Gly Leu Gln Gly Ala Leu Arg Ser Glu Thr	816
260 265 270	
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Gly	Gly	Leu	Ser	Gly	Lys	Pro	Leu	Arg	Asp	Leu	Ser	Thr	Gln	Thr	Ile	
275							280						285			
cgg	gag	atg	tat	gca	ctc	acc	caa	ggc	cga	gtt	ccc	ata	att	ggg	gtt	912
Arg	Glu	Met	Tyr	Ala	Leu	Thr	Gln	Gly	Arg	Val	Pro	Ile	Ile	Gly	Val	
290							295					300				
ggt	ggt	gtg	agc	agc	ggg	cag	gac	gcg	ctg	gag	aag	atc	cgg	gca	ggg	960
Gly	Gly	Val	Ser	Ser	Gly	Gln	Asp	Ala	Leu	Glu	Lys	Ile	Arg	Ala	Gly	
305						310					315					
gcc	tcc	ctg	gtg	cag	ctg	tac	acg	gcc	ctc	acc	ttc	tgg	ggg	cca	ccc	1008
Ala	Ser	Leu	Val	Gln	Leu	Tyr	Thr	Ala	Leu	Thr	Phe	Trp	Gly	Pro	Pro	
320						325				330			335			
gtt	gtg	ggc	aaa	gtc	aag	cgg	gaa	ctg	gag	gcc	ctt	ctg	aaa	gag	cag	1056
Val	Val	Gly	Lys	Val	Lys	Arg	Glu	Leu	Ala	Leu	Leu	Lys	Glu	Gln		
					340				345			350				
ggc	ttt	ggc	gga	gtc	aca	gat	gcc	att	gga	gca	gat	cat	cgg	agg		1101
Gly	Phe	Gly	Gly	Val	Thr	Asp	Ala	Ile	Gly	Ala	Asp	His	Arg	Arg		
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Gln	Gly	Leu	Leu	Asp	Pro	Glu	Ser	Ala	Ala	Arg	Leu	Ala	Val	Arg	Phe	
					20				25			30				
Thr	Ser	Leu	Gly	Leu	Leu	Pro	Arg	Ala	Arg	Phe	Gln	Asp	Ser	Asp	Met	
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Leu	Glu	Val	Arg	Val	Leu	Gly	His	Lys	Phe	Arg	Asn	Pro	Val	Gly	Ile	
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Ala	Ala	Gly	Phe	Asp	Lys	His	Gly	Glu	Ala	Val	Asp	Gly	Leu	Tyr	Lys	
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Met	Gly	Phe	Gly	Phe	Val	Glu	Ile	Gly	Ser	Val	Thr	Pro	Lys	Pro	Gln	
						85			90			95				
Glu	Gly	Asn	Pro	Arg	Pro	Arg	Val	Phe	Arg	Leu	Pro	Glu	Asp	Gln	Ala	
						100			105			110				
Val	Ile	Asn	Arg	Tyr	Gly	Phe	Asn	Ser	His	Gly	Leu	Ser	Val	Val	Glu	
						115			120			125				
His	Arg	Leu	Arg	Ala	Arg	Gln	Gln	Lys	Gln	Ala	Lys	Leu	Thr	Glu	Asp	
						130			135			140				
Gly	Leu	Pro	Leu	Gly	Val	Asn	Leu	Gly	Lys	Asn	Lys	Thr	Ser	Val	Asp	
						145			150			155			160	
Ala	Ala	Glu	Asp	Tyr	Ala	Glu	Gly	Val	Arg	Val	Leu	Gly	Pro	Leu	Ala	
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Asp	Tyr	Leu	Val	Val	Asn	Val	Ser	Ser	Pro	Asn	Thr	Ala	Gly	Leu	Arg	
						180			185			190				
Ser	Leu	Gln	Gly	Lys	Ala	Glu	Leu	Arg	Arg	Leu	Leu	Thr	Lys	Val	Leu	
						195			200			205				
Gln	Glu	Arg	Asp	Gly	Leu	Arg	Arg	Val	His	Arg	Pro	Ala	Val	Leu	Val	
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Lys	Ile	Ala	Pro	Asp	Leu	Thr	Ser	Gln	Asp	Lys	Glu	Asp	Ile	Ala	Ser	
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Val	Val	Lys	Glu	Leu	Gly	Ile	Asp	Gly	Leu	Ile	Val	Thr	Asn	Thr	Thr	
						245			250			255				

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 260 265 270
 Gly Leu Ser Gly Lys Pro Leu Arg Asp Leu Ser Thr Gln Thr Ile Arg
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 290 295 300
 Gly Val Ser Ser Gly Gln Asp Ala Leu Glu Lys Ile Arg Ala Gly Ala
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 Ser Leu Val Gln Leu Tyr Thr Ala Leu Thr Phe Trp Gly Pro Pro Val
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 <211> 1560

<212> DNA

<213> Aspergillus nidulans

<220>
 <221> CDS

<222> (1)...(1560)

<223> Aspergillus nidulans Val200Glu mutant DHODH cDNA

<221> mutation

<222> 599

<223> T to A mutatation

<400> 25

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ctg ggt ggt tgc cgt ctc cca cta acc tgc aga caa ctt cga ttc	96
Leu Gly Gly Cys Arg Arg Leu Pro Leu Thr Cys Arg Gln Leu Arg Phe	
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Ala Ser Asp Ser Gly Ala Ala Ala Thr Thr Lys Ala Thr Ala Glu	
35 40 45	

tca gca gcc gag tca gct agt ata aac gtc aaa gag gca ccc aaa aag	192
Ser Ala Ala Glu Ser Ala Ser Ile Asn Val Lys Glu Ala Pro Lys Lys	
50 55 60	

gcc gga cgg ggc ctg cgg cgc acg gtc ctg gga acg tcg ttg gcg ctg	240
Ala Gly Arg Gly Leu Arg Arg Thr Val Leu Gly Thr Ser Leu Ala Leu	
65 70 75 80	

acg ctg ctg gtt gga tat gtc tac ggg acg gac acc cgg gcg agt gtg	288
Thr Leu Leu Val Gly Tyr Val Tyr Gly Thr Asp Thr Arg Ala Ser Val	
85 90 95	

cat cgg tac ggt gtt gtg ccg ctg att aga gca ttg tat cct gat gcg	336
His Arg Tyr Gly Val Val Pro Leu Ile Arg Ala Leu Tyr Pro Asp Ala	
100 105 110	

gaa gat gcg cat cat att ggt gtc gat act tta aag atg ctg tat aag	384
Glu Asp Ala His His Ile Gly Val Asp Thr Leu Lys Met Leu Tyr Lys	
115 120 125	

tat ggt ctg cat cca agg gaa cgg ggg gat ccg gat gga gat ggg gcg	432
Tyr Gly Leu His Pro Arg Glu Arg Gly Asp Pro Asp Gly Asp Gly Ala	
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Ser Gly Gly Leu Asp Lys His Ala Glu Ile Pro Asp Pro Leu Phe Ala	
165 170 175	
atc ggt cct gcc att gtc gaa gtc ggg ggt acg aca ccc tta cca cag	576
Ile Gly Pro Ala Ile Val Glu Val Gly Gly Thr Thr Pro Leu Pro Gln	
180 185 190	
gat ggt aac ccg cgt cct cgc gaa ttc cga ctt cca tca cag aga gcg	624
Asp Gly Asn Pro Arg Pro Arg Glu Phe Arg Leu Pro Ser Gln Arg Ala	
195 200 205	
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Met Ile Asn Arg Tyr Gly Leu Asn Ser Lys Gly Ala Asp His Met Ala	
210 215 220	
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Ala Ile Leu Glu Gln Arg Val Arg Asp Phe Ala Tyr Ala Asn Gly Phe	
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ggg gca tac gat gcg gct aag cag cgt gta ttg gac ggc gaa gct ggt	768
Gly Ala Tyr Asp Ala Ala Lys Gln Arg Val Leu Asp Gly Glu Ala Gly	
245 250 255	
gtg cca cca ggt agt ctt cag cct ggt aag ctt tta gct gtc caa gtg	816
Val Pro Pro Gly Ser Leu Gln Pro Gly Lys Leu Leu Ala Val Gln Val	
260 265 270	
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Ala Lys Asn Lys Ala Thr Pro Asp Gly Asp Ile Glu Ala Ile Lys Arg	
275 280 285	
gac tat gtg tat tgc gtg gac cgt gtg gcc aaa tac gct gat att ctt	912
Asp Tyr Val Tyr Cys Val Asp Arg Val Ala Lys Tyr Ala Asp Ile Leu	
290 295 300	
gtt gtg aat gta tgc agc ccc aac aca ccc ggt ctc cgt gac ctt caa	960
Val Val Asn Val Ser Ser Pro Asn Thr Pro Gly Leu Arg Asp Leu Gln	
305 310 315 320	
gcc act gcc ccg ctc aca gct atc ttg agt gct gtc gtt ggc gcg gca	1008
Ala Thr Ala Pro Leu Thr Ala Ile Leu Ser Ala Val Val Gly Ala Ala	
325 330 335	
aag agc gtg aac ccg aag acc aaa cca tat gtt atg gtc aag gtc agt	1056
Lys Ser Val Asn Arg Lys Thr Lys Pro Tyr Val Met Val Lys Val Ser	
340 345 350	
ccg gat gaa gac tca gat gaa caa gtc tct ggt atc tgc gac gcc gtc	1104
Pro Asp Glu Asp Ser Asp Glu Gln Val Ser Gly Ile Cys Asp Ala Val	
355 360 365	
cga gca tcc ggt gtc gac gga gtc att gtc gga aac aca aca aac cgt	1152
Arg Ala Ser Gly Val Asp Gly Val Ile Val Gly Asn Thr Asn Arg	

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Arg Pro Asp Pro Ile Pro Gln Gly Tyr Thr Leu	Pro Ala Lys Glu Gln		
385 390	395	400	
gca acg ttg aaa gaa acc ggc ggg tat tca ggt cca	cag ctg ttc gat		1248
Ala Thr Leu Lys Glu Thr Gly Gly Tyr Ser Gly	Pro Gln Leu Phe Asp		
405	410	415	
cgc aca gtg gcc ctt gtg gct cgg tac cgc tcc atg	ctg gat gcg gag		1296
Arg Thr Val Ala Leu Val Ala Arg Tyr Arg Ser Met	Leu Asp Ala Glu		
420	425	430	
tcg gaa acg gcc gga tcc gcc aag gat tca gca gcg	acc ata gcg caa		1344
Ser Glu Thr Ala Gly Ser Ala Lys Asp Ser Ala Ala	Thr Ile Ala Gln		
435	440	445	
aca gag cca ggc tcg gaa aac gtt cct cct gtg gaa	gcg cca agc gga		1392
Thr Glu Pro Gly Ser Glu Asn Val Pro Pro Val Glu	Ala Pro Ser Gly		
450	455	460	
ctg ccg cgc aaa gtt atc ttc gct tcg ggt atc acc	aac ggg aag		1440
Leu Pro Arg Lys Val Ile Phe Ala Ser Gly Gly Ile	Thr Asn Gly Lys		
465	470	475	480
cag gct cac gct gtt tta gac aca ggg gca tct	gtt gcc atg atg tac		1488
Gln Ala His Ala Val Leu Asp Thr Gly Ala Ser Val	Ala Met Met Tyr		
485	490	495	
acc ggt gtg gtc tat ggt ggc gtc ggc act gtc act	cga gtg aag caa		1536
Thr Gly Val Val Tyr Gly Val Gly Thr Val Thr Arg	Val Lys Gln		
500	505	510	
gaa ctt cga acg gcg aaa aag gag			1560
Glu Leu Arg Thr Ala Lys Lys Glu			
515	520		

<210> 26
 <211> 520
 <212> PRT
 <213> Aspergillus nidulans

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 1 5 10 15
 Leu Gly Gly Cys Arg Arg Leu Pro Leu Thr Cys Arg Gln Leu Arg Phe
 20 25 30
 Ala Ser Asp Ser Gly Ala Ala Ala Thr Thr Lys Ala Thr Ala Glu
 35 40 45
 Ser Ala Ala Glu Ser Ala Ser Ile Asn Val Lys Glu Ala Pro Lys Lys
 50 55 60
 Ala Gly Arg Gly Leu Arg Arg Thr Val Leu Gly Thr Ser Leu Ala Leu
 65 70 75 80
 Thr Leu Leu Val Gly Tyr Val Tyr Gly Thr Asp Thr Arg Ala Ser Val
 85 90 95
 His Arg Tyr Gly Val Val Pro Leu Ile Arg Ala Leu Tyr Pro Asp Ala
 100 105 110
 Glu Asp Ala His His Ile Gly Val Asp Thr Leu Lys Met Leu Tyr Lys
 115 120 125
 Tyr Gly Leu His Pro Arg Glu Arg Gly Asp Pro Asp Gly Asp Gly Ala

130	135	140
Leu Ala Thr Glu Val Phe Gly Tyr Thr Leu Ser Asn Pro Ile Gly Ile		
145	150	155
Ser Gly Gly Leu Asp Lys His Ala Glu Ile Pro Asp Pro Leu Phe Ala		160
165	170	175
Ile Gly Pro Ala Ile Val Glu Val Gly Gly Thr Thr Pro Leu Pro Gln		
180	185	190
Asp Gly Asn Pro Arg Pro Arg Glu Phe Arg Leu Pro Ser Gln Arg Ala		
195	200	205
Met Ile Asn Arg Tyr Gly Leu Asn Ser Lys Gly Ala Asp His Met Ala		
210	215	220
Ala Ile Leu Glu Gln Arg Val Arg Asp Phe Ala Tyr Ala Asn Gly Phe		
225	230	235
Gly Ala Tyr Asp Ala Ala Lys Gln Arg Val Leu Asp Gly Glu Ala Gly		240
245	250	255
Val Pro Pro Gly Ser Leu Gln Pro Gly Lys Leu Leu Ala Val Gln Val		
260	265	270
Ala Lys Asn Lys Ala Thr Pro Asp Gly Asp Ile Glu Ala Ile Lys Arg		
275	280	285
Asp Tyr Val Tyr Cys Val Asp Arg Val Ala Lys Tyr Ala Asp Ile Leu		
290	295	300
Val Val Asn Val Ser Ser Pro Asn Thr Pro Gly Leu Arg Asp Leu Gln		
305	310	315
Ala Thr Ala Pro Leu Thr Ala Ile Leu Ser Ala Val Val Gly Ala Ala		320
325	330	335
Lys Ser Val Asn Arg Lys Thr Lys Pro Tyr Val Met Val Lys Val Ser		
340	345	350
Pro Asp Glu Asp Ser Asp Glu Gln Val Ser Gly Ile Cys Asp Ala Val		
355	360	365
Arg Ala Ser Gly Val Asp Gly Val Ile Val Gly Asn Thr Thr Asn Arg		
370	375	380
Arg Pro Asp Pro Ile Pro Gln Gly Tyr Thr Leu Pro Ala Lys Glu Gln		
385	390	395
Ala Thr Leu Lys Glu Thr Gly Gly Tyr Ser Gly Pro Gln Leu Phe Asp		400
405	410	415
Arg Thr Val Ala Leu Val Ala Arg Tyr Arg Ser Met Leu Asp Ala Glu		
420	425	430
Ser Glu Thr Ala Gly Ser Ala Lys Asp Ser Ala Ala Thr Ile Ala Gln		
435	440	445
Thr Glu Pro Gly Ser Glu Asn Val Pro Pro Val Glu Ala Pro Ser Gly		
450	455	460
Leu Pro Arg Lys Val Ile Phe Ala Ser Gly Gly Ile Thr Asn Gly Lys		
465	470	475
Gln Ala His Ala Val Leu Asp Thr Gly Ala Ser Val Ala Met Met Tyr		480
485	490	495
Thr Gly Val Val Tyr Gly Gly Val Gly Thr Val Thr Arg Val Lys Gln		
500	505	510
Glu Leu Arg Thr Ala Lys Lys Glu		
515	520	

<210> 27

<211> 1560

<212> DNA

<213> Aspergillus nidulans

<220>

<221> CDS

<222> (1)...(1560)

<223> Aspergillus nidulans Alall5Val mutant DHODH cDNA

<221> mutation

<222> 344

<223> C to T mutation

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 Met Ala Thr Asn Ser Phe Arg Lys Leu Thr Phe Ser Gly Ala Ser Arg
 1 5 10 15
 ctg ggt ggt tgt cgc cgt ctc cca cta acc tgc aga caa ctt cga ttc
 Leu Gly Gly Cys Arg Arg Leu Pro Leu Thr Cys Arg Gln Leu Arg Phe
 20 25 30
 gcc tcc gac agc gga gcc gca gcg gca act aca aaa gca acg gcc gaa
 Ala Ser Asp Ser Gly Ala Ala Ala Ala Thr Thr Lys Ala Thr Ala Glu
 35 40 45
 tca gca gcc gag tca gct agt ata aac gtc aaa gag gca ccc aaa aag
 Ser Ala Ala Glu Ser Ala Ser Ile Asn Val Lys Glu Ala Pro Lys Lys
 50 55 60
 gcc gga cgg ggc ctg cgg cgc acg gtc ctg gga acg tcg ttg gcg ctg
 Ala Gly Arg Gly Leu Arg Arg Thr Val Leu Gly Thr Ser Leu Ala Leu
 65 70 75 80
 acg ctg ctg gtt gga tat gtc tac ggg acg gac acc cgg gcg agt gtg
 Thr Leu Leu Val Gly Tyr Val Tyr Gly Thr Asp Thr Arg Ala Ser Val
 85 90 95
 cat cgg tac ggt gtt gtg ccg ctg att aga gca ttg tat cct gat gcg
 His Arg Tyr Gly Val Val Pro Leu Ile Arg Ala Leu Tyr Pro Asp Ala
 100 105 110
 gaa gat gtg cat cat att ggt gtc gat act tta aag atg ctg tat aag
 Glu Asp Val His His Ile Gly Val Asp Thr Leu Lys Met Leu Tyr Lys
 115 120 125
 tat ggt ctg cat cca agg gaa cgg ggg gat ccg gat gga gat ggg gcg
 Tyr Gly Leu His Pro Arg Glu Arg Gly Asp Pro Asp Gly Asp Gly Ala
 130 135 140
 ctg gcg aca gag gtc ttt ggg tat aca ctg tca aac cca att ggc ata
 Leu Ala Thr Glu Val Phe Gly Tyr Thr Leu Ser Asn Pro Ile Gly Ile
 145 150 155 160
 tcg ggc ggc ctg gac aag cat gct gag atc cct gat ccg ctg ttc gcg
 Ser Gly Gly Leu Asp Lys His Ala Glu Ile Pro Asp Pro Leu Phe Ala
 165 170 175
 atc ggt cct gcc att gtc gaa gtc ggg ggt acg aca ccc tta cca cag
 Ile Gly Pro Ala Ile Val Glu Val Gly Gly Thr Thr Pro Leu Pro Gln
 180 185 190
 gat ggt aac ccg cgt cct cgc gta ttc cga ctt cca tca cag aga gcg
 Asp Gly Asn Pro Arg Pro Arg Val Phe Arg Leu Pro Ser Gln Arg Ala
 195 200 205
 atg ata aac cgg tac ggc ctc aac tcc aaa ggc gca gat cac atg gca
 Met Ile Asn Arg Tyr Gly Leu Asn Ser Lys Gly Ala Asp His Met Ala
 210 215 220
 gct atc ttg gag caa cga gta cgc gat ttt gcc tac gca aac gga ttt
 Ala Ile Leu Glu Gln Arg Val Arg Asp Phe Ala Tyr Ala Asn Gly Phe
 225 230 235 240

ggg gca tac gat gcg gct aag cag cgt gta ttg gac ggc gaa gct ggt Gly Ala Tyr Asp Ala Ala Lys Gln Arg Val Leu Asp Gly Glu Ala Gly 245 250 255	768
gtg cca cca ggt agt ctt cag cct ggt aag ctt tta gct gtc caa gtg Val Pro Pro Gly Ser Leu Gln Pro Gly Lys Leu Leu Ala Val Gln Val 260 265 270	816
gca aag aac aag gcc act cct gac ggc gac att gaa gcc atc aag cgc Ala Lys Asn Lys Ala Thr Pro Asp Gly Asp Ile Glu Ala Ile Lys Arg 275 280 285	864
gac tat gtg tat tgc gtg gac cgt gtg gcc aaa tac gct gat att ctt Asp Tyr Val Tyr Cys Val Asp Arg Val Ala Lys Tyr Ala Asp Ile Leu 290 295 300	912
gtt gtg aat gta tcg agc ccc aac aca ccc ggt ctc cgt gac ctt caa Val Val Asn Val Ser Ser Pro Asn Thr Pro Gly Leu Arg Asp Leu Gln 305 310 315 320	960
gcc act gcc ccg ctc aca gct atc ttg agt gct gtc gtt ggc gcg gca Ala Thr Ala Pro Leu Thr Ala Ile Leu Ser Ala Val Val Gly Ala Ala 325 330 335	1008
aag agc gtg aac cgc aag acc aaa cca tat gtt atg gtc aag gtc agt Lys Ser Val Asn Arg Lys Thr Lys Pro Tyr Val Met Val Lys Val Ser 340 345 350	1056
ccg gat gaa gac tca gat gaa caa gtc tct ggt atc tgc gac gcc gtc Pro Asp Glu Asp Ser Asp Glu Gln Val Ser Gly Ile Cys Asp Ala Val 355 360 365	1104
cga gca tcc ggt gtc gac gga gtg att gtc gga aac aca aca aac cgt Arg Ala Ser Gly Val Asp Gly Val Ile Val Gly Asn Thr Thr Asn Arg 370 375 380	1152
cgc ccc gac cct ata ccc caa ggt tac act ctt ccg gcc aag gag cag Arg Pro Asp Pro Ile Pro Gln Gly Tyr Thr Leu Pro Ala Lys Glu Gln 385 390 395 400	1200
gca acg ttg aaa gaa acc ggc ggg tat tca ggt cca cag ctg ttc gat Ala Thr Leu Lys Glu Thr Gly Gly Tyr Ser Gly Pro Gln Leu Phe Asp 405 410 415	1248
cgc aca gtg gcc ctt gtg gct cgg tac cgc tcc atg ctg gat gcg gag Arg Thr Val Ala Leu Val Ala Arg Tyr Arg Ser Met Leu Asp Ala Glu 420 425 430	1296
tcg gaa acg gcc gga tcc gcc aag gat tca gca gcg acc ata gcg caa Ser Glu Thr Ala Gly Ser Ala Lys Asp Ser Ala Ala Thr Ile Ala Gln 435 440 445	1344
aca gag cca ggc tcg gaa aac gtt cct cct gtg gaa gcg cca agc gga Thr Glu Pro Gly Ser Glu Asn Val Pro Pro Val Glu Ala Pro Ser Gly 450 455 460	1392
ctg ccg cgc aaa gtt atc ttc gct tcg ggt ggt atc acc aac ggg aag Leu Pro Arg Lys Val Ile Phe Ala Ser Gly Gly Ile Thr Asn Gly Lys 465 470 475 480	1440
cag gct cac gct gtt tta gac aca ggg gca tct gtt gcc atg atg tac	1488

Gln Ala His Ala Val Leu Asp Thr Gly Ala Ser Val Ala Met Met Tyr			
485	490	495	
acc ggt gtc tat ggt ggc gtc ggc act gtc act cga gtc aag caa			
Thr Gly Val Val Tyr Gly Gly Val Gly Thr Val Thr Arg Val Lys Gln			1536
500	505	510	
gaa ctt cga acg gcg aaa aag gag			
Glu Leu Arg Thr Ala Lys Lys Glu			1560
515	520		
<210> 28			
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<213> Aspergillus nidulans			
<400> 28			
Met Ala Thr Asn Ser Phe Arg Lys Leu Thr Phe Ser Gly Ala Ser Arg			
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Leu Gly Gly Cys Arg Arg Leu Pro Leu Thr Cys Arg Gln Leu Arg Phe			
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Ala Ser Asp Ser Gly Ala Ala Ala Thr Thr Lys Ala Thr Ala Glu			
35	40	45	
Ser Ala Ala Glu Ser Ala Ser Ile Asn Val Lys Glu Ala Pro Lys Lys			
50	55	60	
Ala Gly Arg Gly Leu Arg Arg Thr Val Leu Gly Thr Ser Leu Ala Leu			
65	70	75	80
Thr Leu Leu Val Gly Tyr Val Tyr Gly Thr Asp Thr Arg Ala Ser Val			
85	90	95	
His Arg Tyr Gly Val Val Pro Leu Ile Arg Ala Leu Tyr Pro Asp Ala			
100	105	110	
Glu Asp Val His His Ile Gly Val Asp Thr Leu Lys Met Leu Tyr Lys			
115	120	125	
Tyr Gly Leu His Pro Arg Glu Arg Gly Asp Pro Asp Gly Asp Gly Ala			
130	135	140	
Leu Ala Thr Glu Val Phe Gly Tyr Thr Leu Ser Asn Pro Ile Gly Ile			
145	150	155	160
Ser Gly Gly Leu Asp Lys His Ala Glu Ile Pro Asp Pro Leu Phe Ala			
165	170	175	
Ile Gly Pro Ala Ile Val Glu Val Gly Gly Thr Thr Pro Leu Pro Gln			
180	185	190	
Asp Gly Asn Pro Arg Pro Arg Val Phe Arg Leu Pro Ser Gln Arg Ala			
195	200	205	
Met Ile Asn Arg Tyr Gly Leu Asn Ser Lys Gly Ala Asp His Met Ala			
210	215	220	
Ala Ile Leu Glu Gln Arg Val Arg Asp Phe Ala Tyr Ala Asn Gly Phe			
225	230	235	240
Gly Ala Tyr Asp Ala Ala Lys Gln Arg Val Leu Asp Gly Glu Ala Gly			
245	250	255	
Val Pro Pro Gly Ser Leu Gln Pro Gly Lys Leu Leu Ala Val Gln Val			
260	265	270	
Ala Lys Asn Lys Ala Thr Pro Asp Gly Asp Ile Glu Ala Ile Lys Arg			
275	280	285	
Asp Tyr Val Tyr Cys Val Asp Arg Val Ala Lys Tyr Ala Asp Ile Leu			
290	295	300	
Val Val Asn Val Ser Ser Pro Asn Thr Pro Gly Leu Arg Asp Leu Gln			
305	310	315	320
Ala Thr Ala Pro Leu Thr Ala Ile Leu Ser Ala Val Val Gly Ala Ala			
325	330	335	
Lys Ser Val Asn Arg Lys Thr Lys Pro Tyr Val Met Val Lys Val Ser			
340	345	350	

Pro Asp Glu Asp Ser Asp Glu Gln Val Ser Gly Ile Cys Asp Ala Val
 355 360 365
 Arg Ala Ser Gly Val Asp Gly Val Ile Val Gly Asn Thr Thr Asn Arg
 370 375 380
 Arg Pro Asp Pro Ile Pro Gln Gly Tyr Thr Leu Pro Ala Lys Glu Gln
 385 390 395 400
 Ala Thr Leu Lys Glu Thr Gly Tyr Ser Gly Pro Gln Leu Phe Asp
 405 410 415
 Arg Thr Val Ala Leu Val Ala Arg Tyr Arg Ser Met Leu Asp Ala Glu
 420 425 430
 Ser Glu Thr Ala Gly Ser Ala Lys Asp Ser Ala Ala Thr Ile Ala Gln
 435 440 445
 Thr Glu Pro Gly Ser Glu Asn Val Pro Pro Val Glu Ala Pro Ser Gly
 450 455 460
 Leu Pro Arg Lys Val Ile Phe Ala Ser Gly Gly Ile Thr Asn Gly Lys
 465 470 475 480
 Gln Ala His Ala Val Leu Asp Thr Gly Ala Ser Val Ala Met Met Tyr
 485 490 495
 Thr Gly Val Val Tyr Gly Gly Val Gly Thr Val Thr Arg Val Lys Gln
 500 505 510
 Glu Leu Arg Thr Ala Lys Lys Glu
 515 520

<210> 29
 <211> 1707
 <212> DNA
 <213> Mus musculus

<220>
 <221> CDS
 <222> (67)...(1611)
 <223> wild-type IMP dehyrdogenase cDNA

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 gtggtc atg gcg gac tac ctg att agc gga ggc acc tct tac gtg ccg 108
 Met Ala Asp Tyr Leu Ile Ser Gly Gly Thr Ser Tyr Val Pro
 1 5 10

 gac gac ggg ctc aca gcg cag cag ctc ttc aac tgc ggg gac ggc ctc 156
 Asp Asp Gly Leu Thr Ala Gln Gln Leu Phe Asn Cys Gly Asp Gly Leu
 15 20 25 30

 acc tac aat gat ttt ctc att ctt cct ggg tat atc gac ttc act gca 204
 Thr Tyr Asn Asp Phe Leu Ile Leu Pro Gly Tyr Ile Asp Phe Thr Ala
 35 40 45

 gat cag gtg gac ttg acg tct gct cta act aag aag att aca cta aag 252
 Asp Gln Val Asp Leu Thr Ser Ala Leu Thr Lys Lys Ile Thr Leu Lys
 50 55 60

 acc cca ttg gtt tcc tca ccc atg gac act gtc aca gag gct gga atg 300
 Thr Pro Leu Val Ser Ser Pro Met Asp Thr Val Thr Glu Ala Gly Met
 65 70 75

 gcc atc gcg atg gcg ctt aca gga ggt att ggt ttc atc cac cac aac 348
 Ala Ile Ala Met Ala Leu Thr Gly Gly Ile Gly Phe Ile His His Asn
 80 85 90

 tgc aca cct gaa ttc cag gcc aat gaa gtt cgg aaa gtg aag aaa tac 396
 Cys Thr Pro Glu Phe Gln Ala Asn Glu Val Arg Lys Val Lys Lys Tyr
 95 100 105 110

gaa cag gga ttc atc act gac ccc gtg gtc ctt agc ccc aag gat cgt Glu Gln Gly Phe Ile Thr Asp Pro Val Val Leu Ser Pro Lys Asp Arg 115 120 125	444
gta cgc gat gtt ttt gag gcc aaa gcc agg cat ggc ttc tgt ggt atc Val Arg Asp Val Phe Glu Ala Lys Ala Arg His Gly Phe Cys Gly Ile 130 135 140	492
ccc atc aca gat aca ggc cgg atg ggg agt cga ttg gtg ggc atc atc Pro Ile Thr Asp Thr Gly Arg Met Gly Ser Arg Leu Val Gly Ile Ile 145 150 155	540
tcc tca agg gac att gat ttc ctc aag gag gaa gag cat gac cgg ttc Ser Ser Arg Asp Ile Asp Phe Leu Lys Glu Glu His Asp Arg Phe 160 165 170	588
ttg gaa gag atc atg act aag agg gaa gat ttg gtg gtc gcc cct gcc Leu Glu Glu Ile Met Thr Lys Arg Glu Asp Leu Val Val Ala Pro Ala 175 180 185 190	636
ggc gtc act ctg aaa gag gca aat gag att ctg cag cga agt aaa aag Gly Val Thr Leu Lys Glu Ala Asn Glu Ile Leu Gln Arg Ser Lys Lys 195 200 205	684
gga aag ttg ccc att gtg aat gaa aat gat gag ctg gta gcc atc att Gly Lys Leu Pro Ile Val Asn Glu Asn Asp Glu Leu Val Ala Ile Ile 210 215 220	732
gcc cgg aca gac cta aag aag aat cgt gat tac ccc ctg gcc tcc aaa Ala Arg Thr Asp Leu Lys Asn Arg Asp Tyr Pro Leu Ala Ser Lys 225 230 235	780
gat gcc aag aag caa ctg ctg tgt ggg gca gcc att ggc act cat gag Asp Ala Lys Lys Gln Leu Cys Gly Ala Ala Ile Gly Thr His Glu 240 245 250	828
gat gac aag tat agg ctg gac tta ctg gcc ctt gct ggt gtg gat gta Asp Asp Lys Tyr Arg Leu Asp Leu Ala Leu Ala Gly Val Asp Val 255 260 265 270	876
gtg gtt ttg gac tct tcc cag gga aac tcc atc ttc caa atc aat atg Val Val Leu Asp Ser Ser Gln Gly Asn Ser Ile Phe Gln Ile Asn Met 275 280 285	924
atc aaa tac atc aag gag aag tat ccc agt cta cag gtc att gga ggc Ile Lys Tyr Ile Lys Glu Lys Tyr Pro Ser Leu Gln Val Ile Gly Gly 290 295 300	972
aat gta gtc act gct gcg caa gcc aag aac ctc ata gat gca ggt gta Asn Val Val Thr Ala Ala Gln Ala Lys Asn Leu Ile Asp Ala Gly Val 305 310 315	1020
gat gct ttg cga gtc ggc atg gga agt ggt tcc atc tgc atc acc cag Asp Ala Leu Arg Val Gly Met Gly Ser Gly Ser Ile Cys Ile Thr Gln 320 325 330	1068
gaa gtg ttg gcc tgt ggg cgg ccc caa gcc aca gca gtg tac aag gtc Glu Val Leu Ala Cys Gly Arg Pro Gln Ala Thr Ala Val Tyr Lys Val 335 340 345 350	1116
tct gag tat gcc cgt cgc ttt ggt gtt cct gtt att gct gat gga gga	1164

Ser Glu Tyr Ala Arg Arg Phe Gly Val Pro Val Ile Ala Asp Gly Gly			
355	360	365	
atc caa aat gtg ggt cat att gcc aaa gct ttg gct ctt ggg gct tcc		1212	
Ile Gln Asn Val Gly His Ile Ala Lys Ala Leu Ala Leu Gly Ala Ser			
370	375	380	
aca gtc atg atg ggc tcc ctc ctg gct gcc acc act gag gcc cct ggc		1260	
Thr Val Met Met Gly Ser Leu Leu Ala Ala Thr Thr Glu Ala Pro Gly			
385	390	395	
gag tac ttc ttc tca gat ggg atc cgg ctg aag aaa tac cga ggt atg		1308	
Glu Tyr Phe Phe Ser Asp Gly Ile Arg Leu Lys Lys Tyr Arg Gly Met			
400	405	410	
ggt tct ctt gat gcc atg gac aaa cat ctc agc agc cag aac cga tac		1356	
Gly Ser Leu Asp Ala Met Asp Lys His Leu Ser Ser Gln Asn Arg Tyr			
415	420	425	430
ttc agt gaa gct gac aaa atc aaa gtg gcc caa gga gtt tca ggg gca		1404	
Phe Ser Glu Ala Asp Lys Ile Lys Val Ala Gln Gly Val Ser Gly Ala			
435	440	445	
gtg cag gac aag ggg tct atc cac aag ttc gtt cct tac ctg att gct		1452	
Val Gln Asp Lys Gly Ser Ile His Lys Phe Val Pro Tyr Leu Ile Ala			
450	455	460	
ggc atc cag cat tcc tgt caa gac att ggt gcc aag agt tta acc caa		1500	
Gly Ile Gln His Ser Cys Gln Asp Ile Gly Ala Lys Ser Leu Thr Gln			
465	470	475	
gtc aga gcc atg acg tac tcg ggg gag ctt aaa ttt gag aag agg aca		1548	
Val Arg Ala Met Thr Tyr Ser Gly Glu Leu Lys Phe Glu Lys Arg Thr			
480	485	490	
tcc tct gct cag gtg gaa ggt ggc gtc cac agc ctc cat tcg tac gag		1596	
Ser Ser Ala Gln Val Glu Gly Val His Ser Leu His Ser Tyr Glu			
495	500	505	510
aaa cgg ctt ttc tga aaacagatcc agtatatgcc ttgaattttt caataaaagt		1651	
Lys Arg Leu Phe *			
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<212> PRT			
<213> Mus musculus			
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20 25 30			
Asn Asp Phe Leu Ile Leu Pro Gly Tyr Ile Asp Phe Thr Ala Asp Gln			
35 40 45			
Val Asp Leu Thr Ser Ala Leu Thr Lys Lys Ile Thr Leu Lys Thr Pro			
50 55 60			
Leu Val Ser Ser Pro Met Asp Thr Val Thr Glu Ala Gly Met Ala Ile			
65 70 75 80			
Ala Met Ala Leu Thr Gly Gly Ile Gly Phe Ile His His Asn Cys Thr			

85	90	95
Pro Glu Phe Gln Ala Asn Glu Val Arg Lys Val Lys Tyr Glu Gln		
100	105	110
Gly Phe Ile Thr Asp Pro Val Val Leu Ser Pro Lys Asp Arg Val Arg		
115	120	125
Asp Val Phe Glu Ala Lys Ala Arg His Gly Phe Cys Gly Ile Pro Ile		
130	135	140
Thr Asp Thr Gly Arg Met Gly Ser Arg Leu Val Gly Ile Ile Ser Ser		
145	150	155
Arg Asp Ile Asp Phe Leu Lys Glu Glu His Asp Arg Phe Leu Glu		
165	170	175
Glu Ile Met Thr Lys Arg Glu Asp Leu Val Val Ala Pro Ala Gly Val		
180	185	190
Thr Leu Lys Glu Ala Asn Glu Ile Leu Gln Arg Ser Lys Lys Gly Lys		
195	200	205
Leu Pro Ile Val Asn Glu Asn Asp Glu Leu Val Ala Ile Ile Ala Arg		
210	215	220
Thr Asp Leu Lys Lys Asn Arg Asp Tyr Pro Leu Ala Ser Lys Asp Ala		
225	230	235
Lys Lys Gln Leu Leu Cys Gly Ala Ala Ile Gly Thr His Glu Asp Asp		
245	250	255
Lys Tyr Arg Leu Asp Leu Leu Ala Leu Ala Gly Val Asp Val Val Val		
260	265	270
Leu Asp Ser Ser Gln Gly Asn Ser Ile Phe Gln Ile Asn Met Ile Lys		
275	280	285
Tyr Ile Lys Glu Lys Tyr Pro Ser Leu Gln Val Ile Gly Gly Asn Val		
290	295	300
Val Thr Ala Ala Gln Ala Lys Asn Leu Ile Asp Ala Gly Val Asp Ala		
305	310	315
Leu Arg Val Gly Met Gly Ser Gly Ser Ile Cys Ile Thr Gln Glu Val		
325	330	335
Leu Ala Cys Gly Arg Pro Gln Ala Thr Ala Val Tyr Lys Val Ser Glu		
340	345	350
Tyr Ala Arg Arg Phe Gly Val Pro Val Ile Ala Asp Gly Gly Ile Gln		
355	360	365
Asn Val Gly His Ile Ala Lys Ala Leu Ala Leu Gly Ala Ser Thr Val		
370	375	380
Met Met Gly Ser Leu Leu Ala Ala Thr Thr Glu Ala Pro Gly Glu Tyr		
385	390	395
Phe Phe Ser Asp Gly Ile Arg Leu Lys Lys Tyr Arg Gly Met Gly Ser		
405	410	415
Leu Asp Ala Met Asp Lys His Leu Ser Ser Gln Asn Arg Tyr Phe Ser		
420	425	430
Glu Ala Asp Lys Ile Lys Val Ala Gln Gly Val Ser Gly Ala Val Gln		
435	440	445
Asp Lys Gly Ser Ile His Lys Phe Val Pro Tyr Leu Ile Ala Gly Ile		
450	455	460
Gln His Ser Cys Gln Asp Ile Gly Ala Lys Ser Leu Thr Gln Val Arg		
465	470	475
Ala Met Thr Tyr Ser Gly Glu Leu Lys Phe Glu Lys Arg Thr Ser Ser		
485	490	495
Ala Gln Val Glu Gly Gly Val His Ser Leu His Ser Tyr Glu Lys Arg		
500	505	510
Leu Phe		

<210> 31
 <211> 1707
 <212> DNA
 <213> Mus musculus

<220>

<221> CDS
 <222> (67) ... (1611)
 <223> mouse IMP dehydrogenase cDNA double mutant:
 Thr333Ile
 Ser351Tyr

<221> mutation
 <222> 1064
 <223> C to T mutation

<221> mutation
 <222> 1118
 <223> C to A mutation

<400> 31

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Met	Ala	Asp	Tyr	Leu	Ile	Ser	Gly	Gly	Thr	Ser	Tyr	Val	Pro		
1				5					10						

gac	gac	ggg	ctc	aca	gcg	cag	cag	ctc	ttc	aac	tgc	ggg	gac	ggc	ctc	156
Asp	Asp	Gly	Leu	Thr	Ala	Gln	Gln	Leu	Phe	Asn	Cys	Gly	Asp	Gly	Leu	
15				20						25					30	

acc	tac	aat	gat	ttt	ctc	att	ctt	cct	ggg	tat	atc	gac	ttc	act	gca	204
Thr	Tyr	Asn	Asp	Phe	Leu	Ile	Leu	Pro	Gly	Tyr	Ile	Asp	Phe	Thr	Ala	
35					40					45						

gat	cag	gtg	gac	ttg	acg	tct	gtc	cta	act	aag	aag	att	aca	cta	aag	252
Asp	Gln	Val	Asp	Leu	Thr	Ser	Ala	Leu	Thr	Lys	Lys	Ile	Thr	Leu	Lys	
50					55					60						

acc	cca	ttg	gtt	tcc	tca	ccc	atg	gac	act	gtc	aca	gag	gct	gga	atg	300
Thr	Pro	Leu	Val	Ser	Ser	Pro	Met	Asp	Thr	Val	Thr	Glu	Ala	Gly	Met	
65				70					75							

gcc	atc	gcg	atg	gcg	ctt	aca	gga	ggt	att	ggt	ttc	atc	cac	cac	aac	348
Ala	Ile	Ala	Met	Ala	Leu	Thr	Gly	Gly	Ile	Gly	Phe	Ile	His	His	Asn	
80					85				90							

tgc	aca	cct	gaa	ttc	cag	gcc	aat	gaa	gtt	cg	aaa	gtg	aag	aaa	tac	396
Cys	Thr	Pro	Glu	Phe	Gln	Ala	Asn	Glu	Val	Arg	Lys	Val	Lys	Lys	Tyr	
95				100					105			110				

gaa	cag	gga	ttc	atc	act	gac	ccc	gtg	gtc	ctt	agc	ccc	aag	gat	cgt	444
Glu	Gln	Gly	Phe	Ile	Thr	Asp	Pro	Val	Val	Leu	Ser	Pro	Lys	Asp	Arg	
115					120					125						

gta	cgc	gat	gtt	ttt	gag	gcc	aaa	gcc	agg	cat	ggc	ttc	tgt	ggt	atc	492
Val	Arg	Asp	Val	Phe	Glu	Ala	Lys	Ala	Arg	His	Gly	Phe	Cys	Gly	Ile	
130					135					140						

ccc	atc	aca	gat	aca	ggc	cg	atg	ggg	agt	cga	ttg	gtg	ggc	atc	atc	540
Pro	Ile	Thr	Asp	Thr	Gly	Arg	Met	Gly	Ser	Arg	Leu	Val	Gly	Ile	Ile	
145					150					155						

tcc	tca	agg	gac	att	gat	ttc	ctc	aag	gag	gaa	gag	cat	gac	cg	ttc	588
Ser	Ser	Arg	Asp	Ile	Asp	Phe	Leu	Lys	Glu	Glu	Glu	His	Asp	Arg	Phe	
160					165				170							

ttg	gaa	gag	atc	atg	act	aag	agg	gaa	gat	ttg	gtg	gtc	gcc	cct	gcc	636
Leu	Glu	Ile	Met	Thr	Lys	Arg	Glu	Asp	Leu	Val	Val	Ala	Pro	Ala		

175	180	185	190	
ggc gtc act ctg aaa gag gca aat gag att ctg cag cga agt aaa aag				684
Gly Val Thr Leu Lys Glu Ala Asn Glu Ile Leu Gln Arg Ser Lys Lys				
195	200	205		
gga aag ttg ccc att gtg aat gaa aat gat gag ctg gta gcc atc att				732
Gly Lys Leu Pro Ile Val Asn Glu Asn Asp Glu Leu Val Ala Ile Ile				
210	215	220		
gcc cg ^g aca gac cta aag aag aat cgt gat tac ccc ctg gcc tcc aaa				780
Ala Arg Thr Asp Leu Lys Lys Asn Arg Asp Tyr Pro Leu Ala Ser Lys				
225	230	235		
gat gcc aag aag caa ctg ctg tgt ggg gca gcc att ggc act cat gag				828
Asp Ala Lys Lys Gln Leu Leu Cys Gly Ala Ala Ile Gly Thr His Glu				
240	245	250		
gat gac aag tat agg ctg gac tta ctg gcc ctt gct ggt gtg gat gta				876
Asp Asp Lys Tyr Arg Leu Asp Leu Ala Leu Ala Gly Val Asp Val				
255	260	265	270	
gtg gtt ttg gac tct tcc cag gga aac tcc atc ttc caa atc aat atg				924
Val Val Leu Asp Ser Ser Gln Gly Asn Ser Ile Phe Gln Ile Asn Met				
275	280	285		
atc aaa tac atc aag gag aag tat ccc agt cta cag gtc att gga ggc				972
Ile Lys Tyr Ile Lys Glu Lys Tyr Pro Ser Leu Gln Val Ile Gly Gly				
290	295	300		
aat gta gtc act gct gcg caa gcc aag aac ctc ata gat gca ggt gta				1020
Asn Val Val Thr Ala Ala Gln Ala Lys Asn Leu Ile Asp Ala Gly Val				
305	310	315		
gat gct ttg cga gtc ggc atg gga agt ggt tcc atc tgc atc atc cag				1068
Asp Ala Leu Arg Val Gly Met Gly Ser Gly Ser Ile Cys Ile Ile Gln				
320	325	330		
gaa gtg ttg gcc tgt ggg cgg ccc caa gcc aca gca gtg tac aag gtc				1116
Glu Val Leu Ala Cys Gly Arg Pro Gln Ala Thr Ala Val Tyr Lys Val				
335	340	345	350	
tat gag tat gcc cgt cgc ttt ggt gtt cct gtt att gct gat gga gga				1164
Tyr Glu Tyr Ala Arg Arg Phe Gly Val Pro Val Ile Ala Asp Gly Gly				
355	360	365		
atc caa aat gtg ggt cat att gcc aaa gct ttg gct ctt ggg gct tcc				1212
Ile Gln Asn Val Gly His Ile Ala Lys Ala Leu Ala Leu Gly Ala Ser				
370	375	380		
aca gtc atg atg ggc tcc ctc ctg gct gcc acc act gag gcc cct ggc				1260
Thr Val Met Met Gly Ser Leu Leu Ala Ala Thr Thr Glu Ala Pro Gly				
385	390	395		
gag tac ttc ttc tca gat ggg atc cgg ctg aag aaa tac cga ggt atg				1308
Glu Tyr Phe Phe Ser Asp Gly Ile Arg Leu Lys Lys Tyr Arg Gly Met				
400	405	410		
ggt tct ctt gat gcc atg gac aaa cat ctc agc agc cag aac cga tac				1356
Gly Ser Leu Asp Ala Met Asp Lys His Leu Ser Ser Gln Asn Arg Tyr				
415	420	425	430	

ttc agt gaa gct gac aaa atc aaa gtg gcc caa gga gtt tca ggg gca Phe Ser Glu Ala Asp Lys Ile Lys Val Ala Gln Gly Val Ser Gly Ala 435 440 445	1404
gtg cag gac aag ggg tct atc cac aag ttc gtt cct tac ctg att gct Val Gln Asp Lys Gly Ser Ile His Lys Phe Val Pro Tyr Leu Ile Ala 450 455 460	1452
ggc atc cag cat tcc tgt caa gac att ggt gcc aag agt tta acc caa Gly Ile Gln His Ser Cys Gln Asp Ile Gly Ala Lys Ser Leu Thr Gln 465 470 475	1500
gtc aga gcc atg acg tac tcg ggg gag ctt aaa ttt gag aag agg aca Val Arg Ala Met Thr Tyr Ser Gly Glu Leu Lys Phe Glu Lys Arg Thr 480 485 490	1548
tcc tct gct cag gtg gaa ggt ggc gtc cac agc ctc cat tcg tac gag Ser Ser Ala Gln Val Glu Gly Val His Ser Leu His Ser Tyr Glu 495 500 505 510	1596
aaa cgg ctt ttc tga aaacagatcc agtatatgcc ttgaattttt caataaaagt Lys Arg Leu Phe *	1651
ttggaaaaaa aaaagtgaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaa	1707
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Lys Lys Gln Leu Leu Cys Gly Ala Ala Ile Gly Thr His Glu Asp Asp
 245 250 255
 Lys Tyr Arg Leu Asp Leu Leu Ala Leu Ala Gly Val Asp Val Val Val
 260 265 270
 Leu Asp Ser Ser Gln Gly Asn Ser Ile Phe Gln Ile Asn Met Ile Lys
 275 280 285
 Tyr Ile Lys Glu Lys Tyr Pro Ser Leu Gln Val Ile Gly Gly Asn Val
 290 295 300
 Val Thr Ala Ala Gln Ala Lys Asn Leu Ile Asp Ala Gly Val Asp Ala
 305 310 315 320
 Leu Arg Val Gly Met Gly Ser Gly Ser Ile Cys Ile Ile Gln Glu Val
 325 330 335
 Leu Ala Cys Gly Arg Pro Gln Ala Thr Ala Val Tyr Lys Val Tyr Glu
 340 345 350
 Tyr Ala Arg Arg Phe Gly Val Pro Val Ile Ala Asp Gly Gly Ile Gln
 355 360 365
 Asn Val Gly His Ile Ala Lys Ala Leu Ala Leu Gly Ala Ser Thr Val
 370 375 380
 Met Met Gly Ser Leu Leu Ala Ala Thr Thr Glu Ala Pro Gly Glu Tyr
 385 390 395 400
 Phe Phe Ser Asp Gly Ile Arg Leu Lys Lys Tyr Arg Gly Met Gly Ser
 405 410 415
 Leu Asp Ala Met Asp Lys His Leu Ser Ser Gln Asn Arg Tyr Phe Ser
 420 425 430
 Glu Ala Asp Lys Ile Lys Val Ala Gln Gly Val Ser Gly Ala Val Gln
 435 440 445
 Asp Lys Gly Ser Ile His Lys Phe Val Pro Tyr Leu Ile Ala Gly Ile
 450 455 460
 Gln His Ser Cys Gln Asp Ile Gly Ala Lys Ser Leu Thr Gln Val Arg
 465 470 475 480
 Ala Met Thr Tyr Ser Gly Glu Leu Lys Phe Glu Lys Arg Thr Ser Ser
 485 490 495
 Ala Gln Val Glu Gly Gly Val His Ser Leu His Ser Tyr Glu Lys Arg
 500 505 510
 Leu Phe

<210> 33
<211> 5627
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence:Sequence of pMG
plasmid from InvivoGen

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tttgtatgc tattgctta tttgtgaaat ttgtatgct attgcttat ttgtacacc 180
tataagctgc aataacaag ttaacaacaa caattgcatt catttatgt tttaggttca 240
gggggagggtg tgggagggtt tttaaaccaa gtaaaacccct tacaatgtg gtagatccat 300
ttaaatggc ttaagaaca tggagccaa agggccgcaa aaggccagg accgtaaaaaa 360
ggccgcgttg ctggcgttt tccataggct ccgcggccct gacgagcatc acaaaaatcg 420
acgtcaagt cagaggtggc gaaacccgac aggactataa agataccagg cgtttcccc 480
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<211> 40
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Forward primer for amplification-based cloning of hIMPDH type II cDNA

<400> 34
gctatctgca ggccgccacc atggccgact acctgattag 40

<210> 35
<211> 33
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Reverse primer for amplification-based cloning of hIMPDH type II cDNA

<400> 35
catactttc gccaaaaaga ctagatctcg atc 33

<210> 36
<211> 32
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Forward primer for T333I mutation of hIMPDH type II cDNA

<400> 36
ggctccatct gcattatcca ggaagtgcgt gc 32

<210> 37
<211> 32
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Reverse primer for T333I mutation of hIMPDH type II cDNA

<400> 37
ccgaggtaga cgtaataggt cttcacgac cg 32

<210> 38
<211> 38
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Forward primer for S351Y mutation of hIMPDH type II cDNA

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cagcagtgtat caagggttat gagtatgcac ggcgcttt

38

<210> 39

<211> 39

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Reverse primer for S351Y mutation of hIMPDH type II cDNA

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39